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Nutrition and Medication management in home-dwelling older adults

- Associations between nutritional status and drug therapy
- Individual tailored nutritional plan and medication review, an intervention in the malnourished or those at risk

Protocol, 17.12 2019, Mari Fiske, MD, PhD(c)

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ABSTRACT

Malnutrition is common in older adults. The etiology is complex and include unintended medication effects. An increasing number elderly with impaired health live in their own homes, supported by home nursing service and follow-ups from a General Practitioner (GP). Good nutritional status and proper drug treatment can help the older adults to live longer in their own homes, maintaining independence and dignity and reducing the need for space in nursing homes.

The purpose of this study is to investigate the prevalence of malnutrition in older adults (≥70 years), who receives home nursing service in two municipalities, and to explore possible associations between their nutritional status and ongoing drug treatment. Further we will recruit those who are malnourished or at nutritional risk to participate in an interventional follow-up study.

The project consists of two sub-studies:

I. Mapping the nutritional status and medication use of older adults in two municipalities. A cross-sectional study.

II. In older adults, who are malnourished or at nutritional risk, investigate the effect of a composite intervention with an individual nutrition plan and medication review. A pragmatic clinical controlled study.

In order to reach the goal that older adults attain best possible health and quality of life, and allow them to live as long as possible in their own homes, prevention and treatment of malnutrition and to the degree possible optimal medication treatment is paramount. The study is expected to provide knowledge about (a) associations between nutritional status and medication treatment, and (b) effect of a composite intervention consisting of individually tailored nutrition plan to improvement of

their nutritional status and a systematic medication review, specifically evaluating medication with gastro-intestinal / nutritional influence. The intervention study involves multidisciplinary collaboration in primary health care and user participation.

INTRODUCTION

Malnutrition is common in older adults. The etiology is complex and include unintended medication effects (1). An increasing number of elderly with impaired health, remain in their own homes depending on home nursing service and follow-up from their GP (2, 3).

Malnutrition is defined as a situation where the lack of energy, protein and/or other nutrients causes measurable, adverse effects on body composition and functions. The result is weight loss, muscle loss and occasionally altered organ functions (1). Reported incidences of malnutrition in the elderly varies depending on the methods used and the thresholds set for the diagnosis (1). The incidence of malnutrition among home-dwelling older adults ≥ 65 years is around 5 % (4, 5). Among community living persons, who are both old and with impaired health, studies show that around one in ten are malnourished (1), while a further 35 % are at risk of developing malnutrition (6, 7). MNA, Mini Nutritional Assessment, is one of the most widely used, validated nutritional assessment tools for screening in the elderly over 65 years. The short version of MNA, Mini Nutritional Assessment short form, MNA-SF (8, 9), is recommended as a screening tool for home-dwelling older adults (10).

Reduced food intake is the main reason for malnutrition, and may be due to decreased appetite, discomfort or nausea, chewing and/or swallowing problems, disability, cognitive impairment or emotional (e.g. depression) and social conditions (e.g. loneliness). Decreased sense of smell and taste, as well as reduced salivary secretion also plays a major role (11). In addition, for certain diseases, or after injuries or surgeries, the body has increased energy requirements (1). Limited knowledge, interest or attention by health professionals about nutrition and risk of malnutrition, is a major reason for the condition being undiagnosed and treatment interventions starts too late (12, 13). Malnutrition reduces both physical and mental function, increases the risk of complications of illness, delays recovery, reduces quality of life, and is associated with increased mortality (1).

Patients who also suffer from malnutrition are like to stay in hospital up to three times longer than a patient with normal nutritional status (14).

Nutritional therapy is defined as an intervention to alleviate nutrition to meet/satisfy patients' needs for carbohydrates, fats, proteins, vitamins, minerals and trace elements (15). Nutritional treatment for home- dwelling older adults can lead to weight gain, improved functional levels, reduced incidence of falls, and is also likely to have beneficial effects on the immune system (1) as well as hand grip strength (16). In sum, increased focus on prevention and treatment of malnutrition will not only have a positive effect on older adults wellbeing and quality of life, but can also bring about significant improvements in resource utilization and savings in health care (17, 18, 19).

In recent years, malnutrition in older adults has received increasingly more attention. In Norway, "National Guidelines for the Prevention and Treatment of Malnutrition" (10), was published already in 2009, and follow bye "The Diet Manual, a guide in nutrition work in the health and care sector" in 2012 (20). Prevention of malnutrition is an area of focus in the patient safety program (21), and systematic assessment and follow-up of nutrition for patients is established as a national quality indicator for municipal health and care services (22). In 2018 The Norwegian Ministry of Health and Care Services came with a quality reform for older persons, “A full life- all your life” (23). Food and meals is one of the targets. It is also of value to note that The United Nations have proclaimed the decade of Action on Nutrition (2016-2025) (24)

Modern pharmacological treatment helps many older adults, despite illness and/or loss of function, to live active lives and preserve quality of life despite their health problems. Nevertheless, there are many challenges associated with medication treatment. Increasingly, attention is drawn to unintended side effects, questions are raised about negative health effects as a result of medication use and treatment. Normal aging processes alter both the pharmacokinetics and pharmacodynamics of drugs, and these changes are often exacerbated by disease (25). A number of frequently used drugs can cause side effects that cause or contribute to malnutrition. Mouth dryness due to less salvia production and constipation are common among the elderly, and problems increase or are often caused by unintended medication effects, e.g. if agents comes with anticholinergic effects.

Likewise, gastrointestinal ailments such as nausea and discomfort are common medication side effects that can easily result in loss of appetite, anorexia and subsequently weight loss, e.g., use of cholinesterase inhibitors, SSRIs, bisphosphonate or metformin (26). Side effects of medication are often overlooked in the elderly, either because the symptom is perceived as an expression of normal aging or as part of symptoms that follows the known disease or as part of the prescribed medication regime.

Older adults are treated with increasingly sophisticated medication regimes, seen as increasing numbers of medication (27, 28). Polypharmacy denotes the use of many drugs in the same person, however, there is no clear consensus on the definition. Polypharmacy is commonly defined as daily use of five or more drugs, while the use of more than 9-10 drugs daily is often regarded as pronounced polypharmacy (28). A Norwegian study, reported in 2011 showed that 57% of the elderly (≥ 65 years) were prescribed more than five different drugs, while 21% received more than ten different drugs (29) Compared to other European countries, Norway has a relatively low prevalence of polypharmacy (30).

Polypharmacy often involves the use of medications that can be unnecessary or even contraindicated for the patient (31, 32). To guide and alleviate such challenges, the Norwegian General Practice criteria (NORGEP criteria) (33), and the Norwegian General Practice Nursing Home (NORGEP-NH) criteria (34) is developed as a set of explicit criteria for identifying pharmacologically potentially inappropriate prescriptions in general practice for patients over 70 years of age. In this study we choose NORGEP-NH criteria since it is the most updated one, and we consider many of the participants are similar to patients living in nursing homes.

A study based on 2008 data from the Norwegian Prescription Register revealed that 1/3 of home-dwelling older adults, 70 years or older, were prescribed at least one medicine that, based on the NORGEP criteria, could be considered as potentially inappropriate and thus potentially harmful. Of these, one in five received ≥ 10 drugs (31). Misuse and side effects of drugs can be serious and ultimately contribute to, or cause death (35, 36). As part of efforts to reduce inappropriate drug

treatment and reduce the risk of adverse drug effects, systematic drug reviews are recommended (37).

Polypharmacy is associated with poor nutritional status (38). Malnutrition can relate to unintended or adverse drug effects, and is likely to apply primarily to older adults with multiple concurrent diseases and with a comprehensive medication regime. A number of diseases also increase the risk of malnutrition, hence, conclusive evidence about direct or indirect importance of medication treatment to nutritional status can be difficult. However, a Finnish study of home-dwelling older adults, where they adjusted for comorbidity, report that use of more than 9-10 medicines correlated significantly to reduced nutritional status, whereas in those using 6-9 medications the same correlation could not be demonstrated (38).

The relationship between nutritional status, risk or manifest malnutrition, and medication use is not sufficiently explored. To our knowledge, few have previously investigated possible associations between nutritional status and medication use, and in particular possible relationships between inappropriate and potentially harmful medication treatment and nutritional status. Therefor we sat out to examine effects of a composite intervention combining an individualized nutrition plan (nutritional therapy) and measures taken as a result of a critically medication review in people who are malnourished or at nutritional risk.

To contribute to more knowledge in this field, we have defined the following three objectives for the project "Nutrition and Medication management":

For adults (> 70 years) we will:

1. Screen the patients' nutritional status
2. Describe the patients' medication use, incidence of inappropriate drug treatment and use of medicines, potentially leading to loss of appetite, nausea and dry mouth and investigate possible associations between nutritional status and drug treatment.
3. Investigate the impact of a composite intervention with individual nutrition plan and critical medication review on elderly people who are malnourished or at nutritional risk.

"Nutrition and Medication management" is designed as a PhD-project, where these three objectives will be the topic of a scientific article each.

METHODS AND MATERIALS

Subject and setting

The subjects that will be recruited as participants are older adults (≥ 70 years), receiving home care nursing services. They will be recruited from two municipalities in Buskerud County, Norway; Øvre Eiker (ØE) and Nedre Eiker (NE). The municipalities are comparable according to population composition and services for community living older persons with impaired health and function. ØE has approximately 18.500 inhabitants, and NE approximately 24.500 (39). Ø.E has 25 nursing home places in short-time wards and approximately 280 users of home care nursing services. NE has approximately 32 nursing home beds in a short time ward, and 390 receivers of home nursing services. The participants will be recruited by the home nursing services or by a nurse at a short-time ward in the nursing home.

Methods

The project consist of two sub-studies, addressing the objectives, is described separately:

Study I

Nutritional status and medication treatment in home-dwelling older adults

Design

Cross-sectional study

Subject and settings

Older adults (70 +) receiving regular health care from the home nursing service.

Inclusion criteria	Exclusion criteria
• Age 70 + • Receiving home nursing service at least every second week • Medication administrated by home nursing service. • Informed consent by patient or next of kin in case of slightly reduced capacity to consent	• Patient or next of kin refrain from participation or do not wish to participate

Measurements

- **MNA-SF**: Food intake, weight loss, mobility, psychological stress, neuropsychological problems, height and weight according to data collection scheme.
- **Medication in use**: A photo of the medicine prescription card will be taken.

Outcomes

- Nutritional status, assessed by Mini Nutritional Assessment Short Form (MNA-SF)
- Potential Inappropriate medication, assessed by use of the Norwegian General Practice Nursing home (NORGEP-NH) criteria
- Medication with high probably to interact with nutrition; causing nausea, poor appetite or dry mouth will be recorded.

Study II:

Malnutrition in Older Adults. An intervention based on medication review and individual nutritional plan.

Design

Pragmatically controlled clinical study.

Subject and settings

Older adults (70 +) receiving regular health care from the home nursing service and classified as malnourished or at risk of malnutrition, according to MNA-SF.

Inclusion criteria	Exclusion criteria
• Age 70 years or more • Receiving home nursing service at least each second week or more often • Medication administrated by home nursing service. • MNA-SF 0-11 • Informed consent by patient or next of kin	• Life expectance less than 6 months • Serious cognitive impairment or other difficulties for cooperation. • In need of enteral-/parenteral nutrition • Not able to stand up for weight measure • The home nursing service are not responsible for medication administration /delivery • Patient or next of kind do not want to participate

To pragmatically control for spill over between intervention and control group, participants allocated to the intervention group, will be recruited from one municipality (Øvre Eiker) and the control group will be participant from the neighbor municipality (Nedre Eiker). We deem geographic diversion as practical and feasible given available resources, as it could be difficult to manage and avoid spill-over between the two groups of participants, if we make both intervention and control in the same municipality, and especially in the same home nursing district. Based on

the principles of complex interventions (40) we will make a consecutive evaluation of the interventions and if necessary allow for adjustments.

The composite intervention consists has two components (A and B):

Component A: Clinical assessment and critical medication review

Drawing on information from the medical history, clinical finding according to examination made by the principal investigator (trained physician), information from the GP and the findings from blood tests, we will make a systematic and critical medication review. This systematic review has the following considerations:

- Are drug-drug unintended interactions likely to occur? Interaction analysis supported by https:// www.interaksjoner.no
- Are there use of potentially inappropriate medication? Assessed based on the Norwegian General Practice Nursing - Home criteria (NORGEP NH-criteria)
- Could nutritional related problems like loss of appetite, dry mouth, nausea, or constipation be attribute to adverse drug effects? Assessed by the list we made of drugs who often contributes to these side effects according to The Norwegian Pharmaceutical Product Compendium (Felleskatalogen AS) (41).

Component B: Nutritional intervention- individual nutrition plan

Drawing on the principles for good nutritional practice, and the national guidelines, this component include the following considerations:

- Nutritional status by use of MNA-SF, and further in- depth nutrition assessment if MNA-SF in range 0-11.
- Assessment of the nutritional needs.
- Assess food and drink intake with a 3- day dietary record to the estimated nutritional needs.
- In collaboration with the home nurse, the participant and if possible/ necessary a next to kin, focusing on individual problems and develop an individual nutritional plan.

The project is about a controlled implementation of measures recommended in current national guidelines. We will follow a principle known as the "Nutritional Stairs", and choose interventions in the nutritional plan as close to "normal" food as possible. This means that the individual nutritional plan takes into account:

- Physical and mental disorders are diagnosed and optimal treated. (Oral health care included)
- Intervention to optimize the meal environment and meal itself, e.g., enough light in the room, specific tools to make eating possible if necessary, company
- The frequency of meals, length of night fasting, special diets as energy- and nutrient dens diets, consistency customized diet (liquid or solid food)
- Enriched food and in between meals/snacks
- Nutritional supplements

Tabell 1. An overview of the data collection in the intervention (I) and Control group (C).

	Baseline	**4.week**	**12.week**	**24.week**
Medical histories				
Medical historie	I			I
Clinical examination and blood tests.	I			
Admission to hospital and nursing home during the last six months	I/C			I/C
Function				
Heath related quality of life	I/C			I/C
Barthel`s ADL-index	I /C			I/C
Nutrition				
BMI (kg/ $m^{2)}$)	I /C		I	I/C

	Baseline	4.week	12.week	24.week
Nutritional status (MNA-SF)	I /C		I	I/C
Nutritional assessment /nutritional related problems/ nutritional adjustment according to the nutritional plan	I	I	I	
Medication				
Numbers of drugs in use	I/C		I	I/C
Drugs in use with high risk for adverse effect as reduced appetite, dry mouth, nausea	I		I	I/C
Potentially inappropriate medication according to NORGEP-NH-criteria	I/C		I	I/C

The intervention last six months, and participants in the intervention group will receive four visits at home; baseline and after 4, 12 and 24 weeks. At baseline and at week 24, the principal investigator (trained physician) and the nurse will visit the participants. At week 4 and 12, only the nurse will visit them. The control group, are visited by a nurse twice: at baseline and after 24 weeks, and are follow-up by the home nurse service and their GP "as usual".

Drop- out during the study period and reasons for “loss to follow-up (LTFU)” will be registered; e.g., moved from the municipality, acute illness that make further participation difficult, admission to long time ward in nursing home, or any other reason to withdraw participation. In the intervention group, we will on behalf of and subject to the participant’s consent, make an

appointment for consultation by the GP, if the clinical assessment suggests undetected diseases or diseases not optimal treated. If oral health problems are encountered, we will recommend a consultation by a dentist.

Measurements

- ***Mini nutritional assessment short form*** (MNA-SF) (8). Maximal points is 14. 0 -7 points indicates malnutrition. 8-11 points indicate risk for malnutrition. 12-14 points indicates well nourished.
- ***Barthel`s ADL-index*** focus on primary activities of daily living, and consist of ten basic, everyday activities: eating, bath/ shower, personal hygiene items, to get dresses, control of gut and bladder, visit a toilet, move from bed to chair, mobility and to walk up a flight of stairs.
- ***Health related quality of life,*** assessed by one simple question "Consider your health, would you say it is: excellent- very good- good- pretty good- bad.
- ***The Norwegian General Practice Nursing Home (NORGEP-NH) Criteria*** *(34)* for assessing potentially inappropriate medication in use. NORGEP-NH, is developed for use in nursing homes consisting of A: criteria based on single drugs and B) combination criteria and C) a list of prescriptions recommended to be considered for discontinuation (Attachment 1)
- Use of medicines who we considered to cause nausea, loss of appetite or dry mouth will be listed. (Attachment 2) We use The Norwegian Pharmaceutical Product Compendium registry of drugs, (Felleskatalogen AS) (41) and clinical experience.

Outcome

The outcome/effect measures will be analyzed for all included patients, and separately for the groups with malnutrition and nutritional risk.

- ***Primary outcome measure*:** relative and absolute weight change in the individual participant.
- ***Secondary outcome measure:*** Changes in MNA-SF,BMI, p- ADL, health-related quality of life, number of drugs in use, number of drugs considered inappropriate, number of drugs with high risk causing loss of appetite, nausea and dry mouth. In addition, the number of admissions / bed days in hospitals / nursing homes during the project period.

PROCESSING OF DATA

We have created an online solution for collection of these sensitive data, including photos of the medication prescription card. The data will automatically be stored in a secure database at the University of Oslo (TSD). We create a link key to link the personal identified information to the de-identified data. The key linking the participant to the collected research data is stored separately. Further analyses will be performed in the secure database.

STATISTICAL ISSUES - analyses

Primary outcome in study II, changes in body weight, is used to calculate the necessary sample sizes. A mean difference of 5 % is considered to be a clinically relevant difference between the intervention group and the control group. Based on significance level of 0, 05 and power at 80 %, and a SD for intervention/control = 2, 3 / 3, 0, the number of participants is calculated to 40, 20 in the intervention group and 20 in the control group. Five individuals will be added in each group in case of drop-out / LTFU.

Descriptive statistic as frequencies and standard deviations will be used to understand the baseline characteristics of the participants. To understand changes in weight by time, we will use the multiple linear regression model. Estimate of inter-cluster correlation coefficient (ICC) will support considerations of level of variability who characterized the difference between the participations. MNA-SF as score ranged from 0-14, will be categorized in three ordinal categories; 0-7 (malnourish), 8-11 (nutritional risk) and 11-14 (well nourish). To explore factors associated with risk for MNA-SF score, ordinal logistic regression model will be used.

ETHICAL CONSIDERATIONS AND DATA PRIVACY

Participants will provide written, informed consent prior to inclusion in the study. Among the elderly who receive home care nursing, there is high likelihood of varying degrees of cognitive decline/dementia, and reduced consent capacity. At the same time, these individuals belong to a group with particular risk of malnutrition. In the case of inclusion of participants with reduced consent capacity, consent from the next of kin will be obtained. If the patient's cognitive decline is so pronounced that it complicates participation in the project, the person is not included in this study. The control group will receive the follow-up/treatment for patients with nutritional and medication related challenges in the relevant municipality.

The project is about a controlled implementation of measures recommended in current national guidelines. The individualized nutrition plan is knowledge-based, and the measures will not involve any dangers or discomfort to the participants. The critical medication review aims to reduce the risk of drug-related unintended consequences or adverse effects, and is expected to benefit the participants in the intervention group. The GP will be informed about the study before the start and will be informed when their patients are included.

The project is approved by The Norwegian National Committees for Research Ethics, Region South-East B. Approval Number: 2018/1045B. Privacy as well as proper storage and processing of collected data is taken care of through data storage in the TSD.

PROJECT ORGANIZATION / ASSOCIATION

Mari Fiske is a specialist in general medicine, physical medicine and rehabilitation. She is a nursing home physician in a 50 % position in Øvre Eiker municipality. She was appointed as a fellow in 50 % position at the Department of Health and Society, University of Oslo (UiO), 1.2. 2018. Mari Fiske is responsible for conducting the study. She attends the National Research School in General Medicine (NAFALM). Applicant was admitted to the PhD program at the University of Oslo, 27.8.2018. The supervisors are Professor Jørund Strand (general medicine) and Professor Anne Moen (nursing science), both at the Institute for Health and Society, UiO**.**

FUNDING AND TIME SCUDULE

Until November 2019: Under the guidance of Straand and Moen, Mari Fiske has completed work on the study protocol, prepared a web form and collected data from the ØE and NE to study I. Planned assignments in 2018 and 2019 has been postponed due to prolonged absence in connection with serious illness in the immediate family. As of November, 2019, 313 are included in Study I. A start of Study II is scheduled for January 2020. A PhD project with a timeframe of 4 years is planned. The project is financed by the Norwegian Research Fund for General Practice. The aim is to promote a new application to the Research Found annually.

• 2020: MF works in 50% position with project.
• 2021 and 2022: MF works 100% on the project.

The project (by Øvre Eiker municipality) has been granted innovation funds from the County Governor of Buskerud (NOK 350,000). We therefore have the opportunity to "free" personnel from the home care nursing service for work related to the study, as well as hire a nutritionist, etc.

PUBLISHING

The findings from the studies are planned to be published in the form of three articles in international scientific journals (working titles):

- Nutritional status of older adults with home nursing services. A cross-sectional study in two Norwegian municipalities (Study I)
- Associations between drug treatment and nutritional status in older adults with home nursing services. A cross sectional study (Study I).
- Does an intervention composite of Individual Nutrition Plan and critical Medication Review improve nutritional status, functional ability and quality of life, and does the intervention reduce hospital- and nursing- home admissions? A pragmatically controlled clinical study (Study II).

Current authorship rules are followed. In addition to scientific publishing, results and experiences from the project will be communicated to the health and care services in the two municipalities concerned and otherwise in various professional forums and in the media.

STATUS for project work (10.9.2019)

Of 234 included participants from ØE to study I, 9% (21 participants) were malnourished, assessed by MNA-SF. 53.4%, (125 participants) are at nutritional risk. This therefore suggests that it will be possible to include a sufficient number of participants to the intervention group in study II. As of November 2019, 75 participants from Nedre Eiker are included in study I. New users of home services in Øvre Eiker (with start-up services after July 17) will also be included in Study I in fall 2019 and 2020. Scheduled start-up for Study II in January/February 2020.

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Attachment 1:

The Norwegian General Practice Nursing Home (NORGEP-NH) criteria for potentially inappropriate medication use in elderly (>70 years)

A: Singel substance criteria	
Regular use should be avoided	**Comments, adverse effects**
1.Combination analgesic codeine/paracetamol	Poor long-term effects. Constipation, sedation, falls
2.Tricyclic antidepressants (TCAs)[1]	Anticholinergic effects, cardiotoxicity
3.NSAIDs	High risk of side effects and interactions
4. First generation antihistamines[2]	Anticholinergic effects, prolonged sedation
5. Diazepam	Over-sedation, falls, fractures
6. Oxazepam: Dosage >30 mg/day	Over-sedation, falls, fractures
7. Zopiclone: Dosage >5 mg/day	Over-sedation
8. Nitrazepam	Over-sedation, falls, fractures
9. Flunitrazepam	Over-sedation, falls, fractures, addiction
10. Chlometiazole	Poor safety record. Risk of cardiopulmonary death
11. Regular use of hypnotics	Over-sedation, falls, fracture
B: Combination criteria	
Combinations to avoid	
12. Warfarin + NSAIDs	Increased risk of bleeding
13. Warfarin + SSRI/SNRI[3]	Increased risk of bleeding
14. Warfarin + ciprofloxacin/ofloxacin/ erythromycin/ clarithromycin	Increased risk of bleeding
15. NSAIDs/coxibs[4] + ACE-inhibitors[5]/AT2-antagonists[6]	Increased risk of kidney failure
16. NSAIDs/coxibs + diuretics	Reduced effect of diuretics, risk of heart and kidney failure
17. NSAIDs/coxibs + glucocorticoids	Increased risk of bleeding, fluid retention
18. NSAIDs/coxibs + SSRI/SNRIs	Increased risk of bleeding
19. ACE-inhibitors/AT2-antagonists + potassium or potassium- sparing diuretics	potassium-sparing diuretics Increased risk of hyperkalaemia
20. Beta blocking agents + cardioselective calcium antagonists	Increased risk of atrioventricular block, myocardial depression, hypotension, orthostatism
21. Erythromycin/clarithromycin + statins	Increased risk of adverse effects of statins

22. Bisphosphonate + proton pump inhibitors	Increased risk of fractures
23. Concomitant use of three or more psychotropic drugs[7]	Increased risk of falls, impaired memory
24. Tramadol + SSRIs	Risk of serotonin syndrome
25. Metoprolol + paroxetine/fluoxetine/bupropion	Hypotension, orthostatism
26. Metformin + ACE-inhibitors/AT2-antagonists + diuretics	Risk of impaired renal function and metformin-induced lactacidosis, especially in dehydration
C: Deprescribing criteria. Need for continued use should be reassessed [8]:	
27. Anti-psycotics (incl. "atypical" substances[9])	Frequent, serious side effects. avoid long-term use for BPSD[10]
28. Anti-depressants	limited effect on depression in dementia
29. Urologic spasmolytics	limited effect for urinary incontinence in old age risk of anticholinergic side effects
30. Anticholinesterase inhibitors	temporary symptomatic benefits only. Frequent side effect
31. Drugs that lower blood pressure	hypotension, orthostatism, falls
32. Bisphosphonates	assess risk–benefit in relation to life expectancy
33. Statins	assess risk–benefit in relation to life expectancy
34. General use of preventive medication	assess risk–benefit in relation to life expectancy

Notes:1.amitriptyline, doxepine, chlomipramine, trimipramine, nortryptiline; 2.dexchlorfeniramine, promethazine, hydroxyzine, alimemazine (trimeprazine); 3.selective serotonin reuptake inhibitors/selective norepinephrine reuptake inhibitors; 4.cyclooxygenase-2-selective inhibitors; 5.angiotensin-converting enzyme inhibitors; 6.angiotensin II receptor antagonists; 7.from the groups centrally acting analgesics, antipsychotics, antidepressants, and/or benzodiazepines; 8.this should be undertaken at regular intervals. For criteria 27–29, a safe strategy for re-evaluation is first to taper dosage, then stop the drug while monitoring clinical condition; 9.risperidone, olanzapine, quetiapine, aripiprazole; 10.behavioural and psychological symptoms in dementia.

Reference:

Nyborg G, Straand J, Kloving A, Brekke M: The Norwegian General Practice-Nursing home criteria (NORGEP-NH) for potential inappropriate medication use: a web-based Delphi study. Scan. J of Primary care medicine 2015; 33:134-14.

Attachment 2:

Drugs who often contributes to side effects as nausea, loss of appetite and dry mouth (NAD)

ATC			**side effects**	
C03DA01	Spirolakton		Nausea is a prevalent side effect	
M01A	NSAIDs		Risk for gastrointestinal ulceration and nausea can be the main symptom	
	Opioides		Central nausea stimulating effect	
C01AA05	Digoxin		Nausa and loss of appetite. Especially with high serum level	
A06A	Laxatives		Nausea and gastointertinal discomfort	
C013CA01	Diuretics		Nausea and gastointertinal discomfort	
C08	Calsium antagonists		Nausea and gastointertinal discomfort	
C10AA	Statins		Sometimes nausea is a side effect.	
N06A	Antidepressants; (SSRI) Wenlafaxin		Sometimes nausea is a side effect. Frequent gastrointestinal side effects	
J01	Antibiotics		Some antibiotics has a nausea-stimulating effect (erythromycin)	
A10B A	Metformin		Loss of appetite	
M05B A	Bisphosphonates		Erosions in oral cavity and esophagus	
B03A	Iron treatment		Erosions + constipation	
B01AC06	Acetylsalisylic acid		Gastro4intestinal ulcera and erosions	
N06D A	Anticholinesterase inhibitors		Gastrointestinal discomfort	
	The drugs listed below has anticholinergic side effects: **Dry mouth, constipation, cognitive impairment**			**(ADS)**
	Antidepressants			
N06AA04	Anafranil (TCA)	Klomipramin		**3**
N06AA06	Surmontil (TCA)	Trimipramin		**3**
N06AA09	Sarotex (TCA)	Amitryptilin		**3**
N06AA10	Noritren (TCA)	Nortriptilin		**2**

N06AA11	Sinequan (TCA)	Doksepin		**3**
N06AB05	Paroxetin; Seroxat(SSRI)	Paroxetin		**2**
N06AB10	Esitalopram (Cipralex) Citalopram (Cipramil)	Citalopram		**1**
N06AX11	Mirtazapin (Remeron)	Mirtazapin		**1**
	Antipsykotics			
N05AA02	Nozinan	Levopromazin		**3**
N05AB03	Trilafon	Perfenazin		**2**
N05AB04	Stemetil	Proklorperazin		**1**
N05AH02	Clozapin, Leponex	Klozapin		**3**
N05AH03	Olanzapin, ZypAdera, Zyprexa	Olanzepin		**2**
N05AH04	Quantiapin; Seroquel	Quetiapin		**1**
N05AF03	Truxal	Klorprotiksen		**3**
	Antihistamins			
N05BB01	Atarax	Hydralyzin		**3**
R06AB02	Phenamin	Deksklorfenamin		**3**
R06AD01	Vallergan	Alimenazin		**3**
R06AD02	Phenergan	Prometazin		**3**
R06AE05	Postafen	Meklozin		**3**
R06AX13	Loratadin, Clarityn	Loratadin		
	Urologic spasmolytics			
G04BD04	Kentera	Oxybutinin		**2**
G04BD07	Detrusitol	Tolterodin		**3**
G04BD08	Vesicare	Solifenazin		**2**
G04BD10	Emselex	Darifenazin		**1**
G04BD11	Toviaz	Fesoterodin		**3**
G04CA03	Sinalfa	Terazosin		
N02A A/B/E/J/X	**Opiates**			**1**
	C: Cardiovascular system			
C02	Antihypertensiva			
C013CA01	Diuretics ;Furosemid, Diural,Furix,Lasix			**1**
C01DA8/14	Isosorbid; Imdur,Monoket, Sorbangil			**1**
C01AA05	Digoxin			**1**
L01	**L: Antineoplastic drugs:** Imurel, Sandimun			**1**
R01	R: Rhinolytica			**1**
R03A	**R: Antiasthmatics,** adrenergic for inhalation			**1**
N04 B	Parkinson´s medication: Levodopa			**1**
J01	**Antibiotics:**Amoxicillin, ampicillin,gentamycin,klindamycin,piperacillin,vancomycin			**1**

ATC= The Anatomical Therapeutic Chemical Classification System, ADS= Anticholinergic Drug Scale

Ref: Carnahan RM, Lund BC, Perry PJ, Pollock BG, Culp KR. The anticholinergic drug scale as measure of drug- related anticholinergic burden: association with serum anticholinergic activity. J Clin Pharmacol 2006; 46: 1481-86

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